IN THE SPECIFICATION:

(1) Please replace the paragraph that begins at line 19 of page 5 and ends at line 5 of page 6 with the following replacement paragraph:

B1

Much of the coding sequence of the human genome is not homologous to known genes, making detection of open reading frames ("ORFs") and predictions of gene function difficult. Computational methods exist for predicting coding regions in eukaryotic genomes. Gene prediction programs such as GRAIL and GRAIL II, Uberbacher *et al.*, *Proc. Natl. Acad. Sci. USA* 88(24):11261-5 (1991); Xu *et al.*, *Genet. Eng.* 16:241-53 (1994); Uberbacher *et al.*, *Methods Enzymol.* 266:259-81 (1996); GENEFINDER, Solovyev *et al.*, *Nucl. Acids. Res.* 22:5156-63 (1994); Solovyev *et al.*, *Ismb* 5:294-302 (1997); and GENSCAN, Burge *et al.*, *J. Mol. Biol.* 268:78-94 (1997), predict many putative genes without known homology or function. Such programs are known, however, to give high false positive rates. Burset *et al.*, *Genomics* 34:353-367 (1996). Using a consensus obtained by a plurality of such programs is known to increase the reliability of calling exons from genomic sequence. Ansari-Lari *et al.*, Genome Res. 8(1):29-40 (1998).

(2) Please replace the paragraph that begins at line 30 of page 6 and ends at line 9 of page 7 with the following replacement paragraph:

B2

It is common for microarrays to be derived from cDNA/EST libraries, either from those

B2 cont'd

previously described in the literature, such as those from the I.M.A.G.E. consortium, Lennon *et al.*, "The I.M.A.G.E. Consortium: an Integrated Molecular Analysis of Genomes and Their Expression, *Genomics* 33(1):151-2 (1996), or from the construction of "problem specific" libraries targeted at a particular biological question, R.S. Thomas *et al.*, *Toxicologist* 54:68-69 (2000). Such microarrays by definition can measure expression only of those genes found in EST libraries, and thus have not been useful as probes for genes discovered solely by genomic sequencing.

(3) Please replace the paragraph that begins at line 33 of page 23 and ends at line 8 of page 25 with the following replacement paragraph:

B3

As discussed below, and further described in detail in commonly owned and copending U.S. provisional application nos. 60/207,456, filed May 26, 2000; 60/234,687, filed September 21, 2000; 60/236,359, filed September 27, 2000; in commonly owned and copending U.K. patent application no. 0024263.6, filed October 4, 2000; and in commonly owned and copending PCT applications PCT/US01/00666; PCT/US01/00667; PCT/US01/00664; PCT/US01/00669; PCT/US01/00665; PCT/US01/00668; PCT/US01/00663; PCT/US01/00662; PCT/US01/00661; and PCT/US01/00670, the disclosures of which are incorporated herein by reference in their entirety, we have used the methods and apparatus of the present invention to identify more than 15,000 exons in human genomic sequence whose expression we have confirmed in at least one human tissue or cell

B3 Cont'd

type. Fully two-thirds of the exons belong to genes that were not at the time of our discovery represented in existing public expression (EST, cDNA) databases, making the methods and apparatus of the present invention extremely powerful tools for novel gene discovery.

(4) Please replace the paragraph that begins at line 28 of page 76 and ends at line 3 of page 77 with the following replacement paragraph:

B4

One third of the probe sequences (as amplified) produced an exact match (BLAST Expect ("*E*") values less than 1e-100 (1×10^{-100})) to either an EST (20% of sequences) or a known mRNA (13% of sequences). A further 22% of the probe sequences showed some homology to a known EST or mRNA (BLAST *E* values from 1e-5 (1×10^{-5}) to 1e-99 (1×10^{-99})). The remaining 45% of the probe sequences showed no significant sequence homology to any expressed, or potentially expressed, sequences present in public databases.

(5) Please replace the paragraph that begins at line 26 of page 80 and ends at line 10 of page 81 with the following replacement paragraph:

B5

FIG. 7A is a matrix presenting the expression of all verified sequences that showed signal intensity greater than 3 in at least one tissue. Each clone is represented by a column in the matrix. Each of the 10 tissues assayed is represented by a separate row in the matrix, and relative expression (expression ratio) of a clone

B5 cont'd

in that tissue is indicated at the respective node by intensity of green shading, with the intensity legend shown in panel B. The top row of the matrix ("EST Hit") contains "bioinformatic" rather than "physical" expression data – that is, presents the results returned by query of EST, NR and SwissProt databases using the probe sequence. The legend for "bioinformatic expression" (*i.e.*, degree of homology returned) is presented in panel C. Briefly, white is known, black is novel, with gray depicting nonidentical with significant homology (white: *E* values < 1e-100 (1×10^{-100}); gray: *E* values from 1e-5 (1×10^{-5}) to 1e-99 (1×10^{-99}); black: *E* values > 1e-5 (1×10^{-5})).

(6) Please replace the paragraph at lines 7 - 16 of page 82 with the following replacement paragraph:

B6

FIG. 8 shows in dashed line the normalized Cy3 signal intensity for all sequence-verified products with a BLAST Expect ("*E*") value of greater than 1e-30 (1×10^{-30}) (designated "unknown") upon query of existing EST, NR and SwissProt databases, and shows in solid line the normalized Cy3 signal intensity for all sequence-verified products with a BLAST Expect value of less than 1e-30 (1×10^{-30}) ("known"). Note that biological background noise has an averaged normalized Cy3 signal intensity of 0.2.

(7) Please replace the paragraph that begins at line 18 of page 96 and ends at line 22 of page 97 with the following replacement paragraph:

B7

Using this threshold, we identified over 15,000 single exon probes that produce significant signal in one or more of ten tested tissues/cell types. The exact structures of these single exon probes are clearly presented in the SEQUENCE LISTINGs included in commonly owned and copending U.S. provisional application nos. 60/207,456, filed May 26, 2000; 60/234,687, filed September 21, 2000; 60/236,359, filed September 27, 2000; in commonly owned and copending U.K. patent application no. 0024263.6, filed October 4, 2000; and in commonly owned and copending PCT applications PCT/US01/00666; PCT/US01/00667; PCT/US01/00664; PCT/US01/00669; PCT/US01/00665; PCT/US01/00668; PCT/US01/00663; PCT/US01/00662; PCT/US01/00661; and PCT/US01/00670, the disclosures of which are incorporated herein by reference in their entireties.

(8) Please replace the paragraph that begins at line 12 of page 98 and ends at line 13 of page 99 with the following replacement paragraph:

B8

The exact structures of these single exon probes are clearly presented in the SEQUENCE LISTINGs included in commonly owned and copending U.S. provisional application nos. 60/207,456, filed May 26, 2000; 60/234,687, filed September 21, 2000; 60/236,359, filed September 27, 2000; in commonly owned and copending U.K. patent application no. 0024263.6, filed October 4, 2000; and in commonly owned and copending PCT applications PCT/US01/00666; PCT/US01/00667; PCT/US01/00664; PCT/US01/00669; PCT/US01/00665; PCT/US01/00668;